

REMARKS

Claims 1-44 are pending in the instant application. Claims 1-32, 34, and 36, 37 and 39 are rejected. Claims 33, 35, 38 and 40-44 are withdrawn from consideration. Applicants are responding within two months of a Final Rejection and look forward to an Advisory Action or Notice of Allowance. Applicants herein amend claim 1 to clarify that the units of the percentages are by weight, to remove the 68% to 32% and replace it with the 68:32 proportion expressed in the specification and to replace “proportional” with “a proportion” to express how the 4GPX is related to the amount of 2GPX and 3GPX. No issue of new matter arises by way of these changes as the changes are merely semantic and clarify what is clearly taught in the specification. In addition, Applicants clarify claim 1, step (v) to recite that the isolating fractions is performed by a method selected from the group consisting of addition of celite to the fourth reaction mixture, followed by solid-liquid extraction with a solvent and elution with a first eluent in a column *wherein the first eluent is a mixture of water/isopropanol that contains 1 to 10% (v/v) of isopropanol*; and directly adding active carbon to the fourth reaction mixture followed by filtration and elution with a second eluent. The additional recitation is intended to more clearly describe the isolating step and effectively combines claims 1 and 5 such that no issue of new matter arises by way of this change. As such, Applicants herein cancel claim 5 as not further limiting claim 1 so that upon entry of the instant Amendment, claims 1-4 and 6-44 will be pending, claims 1-4, 6-32, 34, and 36, 37 and 39 will be rejected, and claims 33, 35, 38 and 40-44 will remain withdrawn from consideration.

Rejection under 35 USC 112, second paragraph

The Examiner now rejects all of the claims being examined as unclear because of the language that Applicants introduced into claim 1 in the last Amendment and Response “producing 4GPX...in an amount at least 68% to 32% proportional to the amount of 2GPX and 3 GPX.”

The Examiner provides the following reasons:

1. It does not define the units of the percentages, i.e. weight, volume, mole/mole, weight/volume, etc.;
2. “at least 68% to 32%” is open ended;
3. “proportional” is unclear because it is unclear how the proportion of 4GPX is related to the amount of 2GPX and 3GPX.

Applicants herein clarify this language to more clearly describe what is intended. Applicants rely upon paragraph [0049] for support for the 68:32 ratio. This value was generated by gas chromatography analysis. One of ordinary skill in the art would readily appreciate that the units are expressed by weight. Further, “proportional” is changed to read “a proportion” thereby clarifying the language and representing no more than a semantic issue.

Rejection under 35 USC 103

1. *Reyes et al.*, U.S. Patent 5,994,092 in view of *Ponpipom et al.*, U.S. Patent 4,228,274 and *Crompton et al.*, *Biochem. J.* 70(4):729 (1958)

The Examiner maintains the rejection of claims 1-4, 21-24, 27-32, 34, 36, 37 and 39 as unpatentable over *Reyes et al.*, U.S. Patent 5,994,092 in view of *Ponpiporn et al.*, U.S. Patent 4,228,274 and *Crompton et al.*, *Biochem. J.* 70(4):729 (1958) as before. The Examiner says that steps (v) and (vi) are obvious over these references. However, the Examiner appears to indicate that the claims will be patentable over these references once the scope of claim 1 is clarified as noted with the rejection under 35 U.S.C. 112, second paragraph.

2. *Reyes et al.*, U.S. Patent 5,994,092 in view of *Ponpipom et al.*, U.S. Patent 4,228,274 and *Crompton et al.*, *Biochem. J.* 70(4):729 (1958) supported by *Schippers et al.*, (*Analytical Chem.* 1981)

The Examiner rejects claims 1-4, 21-24, 27-32, 34, 36, 37 and 39 as unpatentable over *Reyes et al.*, U.S. Patent 5,994,092 in view of *Ponpiporn et al.*, U.S. Patent 4,228,274 and

Crumpton *et al.*, *Biochem. J.* 70(4):729 (1958) as before supported by Schippers *et al.*, (*Analytical Chem.* 1981. However, the Examiner appears to indicate that the claims will be patentable over these references once the scope of claim 1 is clarified as noted with the rejection under 35 U.S.C. 112, second paragraph.

3. *Reyes et al.*, U.S. Patent 5,994,092 in view of Ponpipom *et al.*, U.S. Patent 4,228,274 and Crumpton *et al.*, *Biochem. J.* 70(4):729 (1958) further in view of Wong-Madden *et al.*, U.S. Patent 5,770,405 and Dahmen *et al.*, U.S. Patent 4,675,392

The Examiner maintains the rejection of claims 1, 5, 6 and 16-19 as unpatentable over Reyes *et al.*, U.S. Patent 5,994,092 in view of Ponpipom *et al.*, U.S. Patent 4,228,274 and Crumpton *et al.*, *Biochem. J.* 70(4):729 (1958) further in view of Wong-Madden *et al.*, U.S. Patent 5,770,405 and Dahmen *et al.*, U.S. Patent 4,675,392. However, the Examiner appears to indicate that the claims will be patentable over these references once the scope of claim 1 is clarified as noted with the rejection under 35 U.S.C. 112, second paragraph.

4. *Reyes et al.*, U.S. Patent 5,994,092 in view of Ponpipom *et al.*, U.S. Patent 4,228,274 and Crumpton *et al.*, *Biochem. J.* 70(4):729 (1958) further in view of Wong-Madden *et al.*, U.S. Patent 5,770,405 and Dahmen *et al.*, U.S. Patent 4,675,392 and further in view of Rao *et al.*, *Qual. Plant.-Pl. Fds. Hum. Nutr.* XXVIII 4:293-303 (1979)

The Examiner maintains the rejection of claims 1 and 7-15 as unpatentable over Reyes *et al.*, U.S. Patent 5,994,092 in view of Ponpipom *et al.*, U.S. Patent 4,228,274 and Crumpton *et al.*, *Biochem. J.* 70(4):729 (1958) further in view of Wong-Madden *et al.*, U.S. Patent 5,770,405 and Dahmen *et al.*, U.S. Patent 4,675,392 and further in view of Rao *et al.*, *Qual. Plant.-Pl. Fds. Hum. Nutr.* XXVIII 4:293-303 (1979). However, the Examiner appears to indicate that the claims will be patentable over these references once the scope of claim 1 is clarified as noted with the rejection under 35 U.S.C. 112, second paragraph.

5. *Reyes et al.*, U.S. Patent 5,994,092 in view of Ponpipom *et al.*, U.S. Patent 4,228,274, Crumpton *et al.*, *Biochem. J.* 70(4):729 (1958), Dahmen *et al.*, U.S. Patent 4,675,392,

Rao et al., Qual. Plant.-Pl. Fds. Hum. Nutr. XXVIII 4:293-303 (1979) and Wong-Madden et al., U.S. Patent 5,770,405 in further view of Gabelsberger et al., FEMS Letters 109(2-3): 131 (1993), Fujimoto et al., Glycoconjugate Journal 15:155 (1998) and Yoshitake et al., Eur. J. Biochem. 101:395 (1979).

The Examiner maintains the rejection of claims 25 and 26 as unpatentable over this combination. However, the Examiner appears to indicate that the claims will be patentable over these references once the scope of claim 1 is clarified as noted with the rejection under 35 U.S.C. 112, second paragraph.

Previously submitted explanations

Applicants reiterate that the present invention provides an improved enzymatic process in order to increase the proportion of 4-O- β -D-galactopyranosyl-D-xylose product with respect to the 2- and 3-O- β -D-galactopyranosyl-D-xylose products in the final mixture. The examples in the specification demonstrate that this results in a yield at 37°C of 71:29 (4-O- β -D-galactopyranosyl-D-xylose/ (2-O- β -D-galactopyranosyl-D-xylose)). *See*, Table 1. None of the cited prior art teaches or suggests adding the fractionation steps (v) and (vi) as recited in the currently pending claims. Even if, *assuming arguendo*, the prior art did teach such fractionation steps, the present invention would still be patentable because the prior art does not teach or suggest a process resulting in such a high yield of 4-O- β -D-galactopyranosyl-D-xylose in proportion to the 2-O- β -D-galactopyranosyl-D-xylose and 3-O- β -D-galactopyranosyl-D-xylose.

Applicants further submit that disaccharides 2-, 3-, and 4- are regloisomers (position isomers) having similar physical and chemical properties. Therefore, the separation of each isomer from the whole mixture is difficult since they share similar physical and chemical properties. *See, e.g.* Second Declaration under 37 C.F.R. 1.132 of Dr. Alfonso Fernandez-Mayoralas Alvarez, paragraphs 6 and 7. Yet, separating these isomers is very important because the 2- and 3- isomers do not work properly in an intestinal lactase test in which the 4- isomer is used.

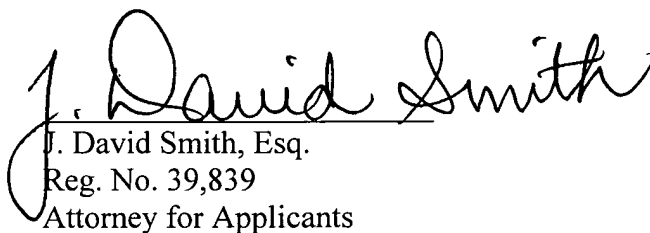
The present invention provides a method for separating the isomers that the prior art does not teach or suggest. A surprisingly good 4:2+3 isomer ratio is achieved by the presently claimed process. This surprising ratio may be achieved due to the activity of the galactosidase

enzyme of *E. coli*. The surprising ratio achieved ranges from 68:32 to 83:17 depending upon the temperature or pH conditions. When physiological conditions were used (37°C at pH 7.0), the ratio of 4:2+3 isomer was 71:29. An increased ratio of 4:2+3 isomer was observed when the temperature or the pH was lower than physiological conditions. *See*, Tables 1 and 2 of the instant specification. However, for many reasons, it may be preferable to use physiological conditions. Moreover, the purity of the 4-isomer separated by the presently claimed process was greater than 99%. *See, e.g.* Second Declaration under 37 C.F.R. 1.132 of Dr. Alfonso Fernandez-Mayoralas Alvarez, paragraph 10. Applicants herein combine claims 1 and 5 so that claim 1 now reads more closely in line with the specific protocol used to produce the unexpectedly superior results discussed.

CONCLUSION

Entry of the foregoing amendments and remarks is respectfully requested. It is believed that all of the claims are in condition for allowance. If any issue can be resolved telephonically, the Examiner is invited to call the undersigned at the phone number provided.

Respectfully submitted,


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